

CLAIMS

What is claimed is:

1. An isolated and purified biologically active MAT II β subunit polypeptide having MAT II modulating activity.
- 5 2. The polypeptide of claim 1, wherein the polypeptide comprises a vertebrate MAT II β subunit polypeptide.
3. The polypeptide of claim 2, wherein the polypeptide comprises a human MAT II β subunit polypeptide.
4. The polypeptide of claim 3, wherein the MAT II β subunit
10 comprises an amino acid sequence as essentially set forth in any of Figures 1-5.
5. The polypeptide of claim 1, modified to be in detectably labeled form.
6. An isolated and purified antibody capable of specifically binding
15 to the polypeptide of claim 1.
7. The antibody of claim 6 which is a monoclonal antibody.
8. The antibody of claim 6 which is a polyclonal antibody.
9. A hybridoma cell line which produces the monoclonal antibody of claim 8.
- 20 10. An isolated and purified antibody capable of neutralizing the biological activity of the polypeptide of claim 1.
11. The antibody of claim 10 which is a monoclonal antibody.
12. The antibody of claim 10 which is a polyclonal antibody.

13. A hybridoma cell line which produces the monoclonal antibody of claim 11.

14. An isolated and purified polynucleic acid encoding a biologically active MAT II β subunit polypeptide capable of modulating MAT II biological activity.

15. The polynucleic acid of claim 14, wherein the encoded polypeptide comprises a vertebrate MAT II β subunit polypeptide.

16. The polynucleic acid of claim 15, wherein the encoded polypeptide comprises a mammalian MAT II β subunit polypeptide.

17. The polynucleic acid of claim 16, wherein the encoded polypeptide comprises a human MAT II β subunit polypeptide.

18. The polynucleic acid of claim 14, wherein the encoded polypeptide comprises an amino acid sequence as essentially set forth in any of Figures 1-5.

19. The polynucleic acid of claim 18, further defined as comprising a MAT II β subunit-encoding polynucleic acid as essentially set forth in any of Figures 1-5.

20. The polynucleic acid of claim 14, further defined as a DNA segment.

21. The polynucleic acid of claim 14, further defined as positioned under the control of a promoter.

22. The polynucleic acid of claim 14, further defined as a recombinant vector.

23. The polynucleic acid of claim 22, wherein the vector is a recombinant expression vector.

24. The polynucleic acid of claim 22, further defined as a nucleic acid fragment of up to 10,000 basepairs in length.

5 25. The polynucleic acid of claim 24, further defined as comprising at least a 1000 nucleotide long contiguous stretch of a polynucleic acid sequence as essentially set forth in any of Figures 1-5.

26. A recombinant host cell comprising the polynucleic acid of claim 14.

10 27. The recombinant host cell of claim 26, wherein the host cell is a procaryotic cell.

28. The recombinant host cell of claim 26, wherein the host cell is a eukaryotic cell.

15 29. A method of preparing a MAT II β subunit polypeptide, comprising: transforming a cell with the polynucleic acid of claim 14 to produce a MAT II β subunit under conditions suitable for the expression of said polypeptide.

20 30. A method of detecting in a sample an RNA that encodes the MAT II β subunit polypeptide encoded by the nucleic acid of claim 14, said method comprising the steps of:

- (a) contacting said sample under hybridizing conditions with the polynucleic acid of claim 14 to form a duplex; and
- (b) detecting the presence of said duplex.

31. A method of producing an antibody immunoreactive with a MAT II β subunit polypeptide, the method comprising steps of:

- (a) transfecting a recombinant host cell with the a polynucleic acid of claim 14, which encodes a MAT II β subunit polypeptide;
- 5 (b) culturing the host cell under conditions sufficient for expression of the polypeptide;
- (c) recovering the polypeptide; and
- (d) preparing the antibody to the polypeptide.

10 32. The method of claim 31, wherein the polypeptide comprises a polypeptide as essentially set forth in any of Figures 1-5.

33. The method of claim 31, wherein the polynucleic acid comprises a polynucleic acid sequence as essentially set forth in any of Figures 1-5.

34. An antibody produced by the method of claim 31.

15 35. A method of detecting a MAT II β subunit polypeptide, the method comprising immunoreacting the polypeptide with an antibody prepared according the method of claim 31 to form an antibody-polypeptide conjugate; and detecting the conjugate.

20 36. A method of detecting a messenger RNA transcript that encodes a MAT II β subunit polypeptide, the method comprising the steps of hybridizing the messenger RNA transcript with the polynucleic acid of claim 14 to form a duplex; and detecting the duplex.

37. A method of detecting a DNA molecule that encodes a MAT II β subunit polypeptide, the method comprising the steps of hybridizing DNA

molecules with the polynucleic acid of claim 14 to form a duplex; and detecting the duplex.

38. An assay kit for detecting the presence of a MAT II β subunit polypeptide in a biological sample, the kit comprising a first container
5 containing a first antibody capable of immunoreacting with a MAT II β subunit polypeptide of claim 1, wherein the first antibody is present in an amount sufficient to perform at least one assay.

39. The assay kit of claim 38, further comprising a second container containing a second antibody that immunoreacts with the first antibody.

10 40. The assay kit of claim 39, wherein the first antibody and the second antibody comprise monoclonal antibodies.

41. The assay kit of claim 39, wherein the first antibody is affixed to a solid support.

15 42. The assay kit of claim 39, wherein the first and second antibodies each comprise an indicator.

43. The assay kit of claim 42, wherein the indicator is a radioactive label, a fluorescent label or an enzyme.

20 44. An assay kit for detecting the presence, in biological samples, of a MAT II β subunit polypeptide, the kit comprising a first container that contains a polynucleic acid identical or complimentary to a segment of at least ten contiguous nucleotide bases of the polynucleic acid of claim 14.

45. An assay kit for detecting the presence, in a biological sample, of an antibody immunoreactive with a MAT II β subunit polypeptide, the kit comprising a first container containing a MAT II β subunit polypeptide of claim

1 that immunoreacts with the antibody, with the polypeptide present in an amount sufficient to perform at least one assay.

46. A method of screening candidate substances for an ability to modulate MAT II β subunit biological activity, the method comprising the steps
5 of:

- (a) establishing replicate test and control cell samples that comprise and a biologically active MAT II β subunit polypeptide;
- (b) administering a candidate substance to the test sample
10 but not the control sample;
- (c) measuring cell growth in the test and the control samples; and
- (d) determining that the candidate substance modulates MAT II β subunit biological activity if the cell growth measured
15 for the test sample is greater or less than the cell growth measured for the control sample.

47. The method of claim 46, wherein the candidate substance is further characterized as a candidate polypeptide, and further comprising the step of purifying and isolating a gene encoding the candidate polypeptide.

20 48. The method of claim 46, wherein the replicate test and control samples further comprise a cell that expresses a vertebrate MAT II β subunit polypeptide capable of modulating MAT II biological activity.

49. A recombinant cell line suitable for use in the method of claim 46.

50. A method of modulating MAT II β subunit polypeptide activity in a vertebrate subject, the method comprising the step of administering to the vertebrate subject an effective amount of a substance capable of modulating the MAT II β subunit polypeptide activity in the vertebrate subject, whereby modulation of the MAT II β subunit polypeptide activity is accomplished.

51. The method of claim 50, wherein the step of administering further comprises administering an effective amount of a substance that modulates expression of a MAT II β subunit-encoding polynucleic acid in the vertebrate.

52. The method of claim 51, wherein the substance that modulates expression of a MAT II β subunit-encoding polynucleic acid comprises an antisense oligonucleotide.

53. The method of claim 50, where the substance that modulates the MAT II β subunit activity comprises an anti-MAT II β subunit antibody.

54. The method of claim 53, where the anti-MAT II β subunit antibody comprises a monoclonal antibody.

55. The method of claim 50, wherein the MAT II β subunit activity comprises modulating MAT II biological activity, and wherein the step of administering comprises administering to the vertebrate an effective MAT II β subunit-modulating amount of a substance capable of modulating MAT II β subunit modulation of MAT II biological activity.

56. The method of claim 50, wherein the vertebrate is a mammal.

57. The method of claim 56, wherein the mammal is a human.

58. A method of treating a patient suffering from a disorder associated with MAT II biological activity in the patient, the method comprising the steps of:

- (a) administering to the patient an effective amount of a substance capable of modulating MAT II β subunit activity in the patient, whereby modulation of the MAT II β subunit polypeptide activity is accomplished; and
- (b) modulating MAT II biological activity in the patient through the modulation of the MAT II β subunit activity, whereby treatment of the disorder is accomplished.

59. The method of claim 58, wherein the step of administering further comprises administering an effective amount of a substance that modulates expression of a MAT II β subunit-encoding polynucleic acid in the patient.

60. The method of claim 59, wherein the substance that modulates expression of a MAT II β subunit-encoding polynucleic acid comprises an antisense oligonucleotide.

61. The method of claim 58, wherein the substance capable of modulating MAT II β subunit activity in the vertebrate comprises an anti-MAT II β subunit antibody.

62. The method of claim 61, wherein the anti-MAT II β subunit antibody comprises a monoclonal antibody.

63. A method of treating a patient suffering from a disorder associated with MAT II biological activity in the patient, the method comprising the step of administering to the patient a therapeutic composition which

comprises a biologically active MAT II β subunit polypeptide, whereby treatment of disorder associated with MAT II biological activity in the patient is accomplished.

64. The method of claim 63, wherein the modulated MAT II biological activity comprises MAT II biological activity endogenous to the vertebrate subject.

65. The method of claim 63, wherein the modulated MAT II biological activity comprises MAT II biological activity in bacterial, fungal or other parasitic cells residing in the vertebrate subject, to thereby treat infection of the patient by said organisms.

66. The method of claim 63, wherein the therapeutic composition comprises a MAT II β subunit polypeptide as essentially set forth in any of Figures 1-5 and a pharmaceutically acceptable carrier.

67. A method for modulating MAT II biological activity in a cell comprising the steps of:

- (a) delivering to the cell an effective amount of a DNA molecule comprising a polynucleotide that encodes a MAT II β subunit polypeptide that modulates MAT II biological activity; and
- (b) maintaining the cell under conditions sufficient for expression of said polypeptide.

68. The method of claim 67, wherein the polypeptide comprises a polypeptide as essentially set forth in any of Figures 1-5.

69. The method of claim 67, wherein the polynucleotide comprises a polynucleic acid sequence as essentially set forth in any of Figures 1-5.

70. A transgenic non-human animal having incorporated into its genome a polynucleic acid encoding a biologically active MAT II β subunit polypeptide capable of modulating MAT II biological activity; the polynucleic acid being present in said genome in a copy number effective to confer expression in the animal of the MAT II β subunit polypeptide.

71. The transgenic non-human animal of claim 70, wherein said polynucleic acid is further defined as a human MAT II β subunit-encoding segment.

72. A method for identifying a candidate compound as a therapeutic agent in the modulation of MAT II β biological activity, the method comprising the steps of:

- (a) contacting a cell sample with a predetermined concentration of the candidate compound to be tested, the cell sample comprising at least one cell comprising a DNA construct comprising in 5' to 3' order (i) a modulatable transcriptional regulatory sequence of a MAT II β subunit-encoding gene, (ii) a promoter of the MAT II β subunit-encoding gene, and (iii) a reporter gene which expresses a polypeptide capable of producing a detectable signal coupled to and under the control of the promoter, under conditions such that the candidate compound if capable of acting as a transcriptional modulator of the gene encoding the protein of interest, causes a measurable detectable signal to be produced by the polypeptide expressed by the reporter gene;
- (b) quantitatively determining the amount of the signal so produced;

- (c) comparing the amount so determined with the amount of produced signal detected in the absence of candidate compound being tested or upon contacting the cell sample with other compounds so as to thereby identify the candidate compound as a chemical which causes a change in the detectable signal produced by the polypeptide and which transcriptionally modulates expression of MAT II β subunit; and
- (d) identifying the candidate compound as a therapeutic agent in the modulation of MAT II β subunit biological activity if the candidate compound transcriptionally modulates expression of MAT II β subunit.

73. A method for identifying a compound as a therapeutic agent in the modulation of MAT II β subunit biological activity, the method comprising the steps of:

- (a) contacting a cell sample with a predetermined concentration of the candidate compound to be tested, the cell sample comprising at least one cell comprising a DNA construct comprising in 5' to 3' order (i) a modulatable transcriptional regulatory sequence of a MAT II β subunit-encoding gene, (ii) a promoter of the MAT II β subunit-encoding gene, and (iii) a DNA sequence transcribable into mRNA coupled to and under the control of the promoter, under conditions such that the candidate compound if capable of acting as a transcriptional modulator of the MAT II β subunit-

encoding gene, causes a measurable difference in the amount of mRNA transcribed from the DNA sequence;

- (b) quantitatively determining the amount of the mRNA so produced;
- (c) comparing the amount so determined with the amount of mRNA detected in the absence of candidate compound being tested or upon contacting the cell sample with other compounds so as to thereby identify the candidate compound as a compound which causes a change in the detectable mRNA amount and which transcriptionally modulates expression of MAT II β subunit; and
- (d) identifying the candidate compound as a therapeutic agent in the modulation of MAT II β subunit biological activity if the candidate compound transcriptionally modulates expression of MAT II β subunit.

74. The method of claim 72, which comprises separately contacting each of a plurality of identical cell samples with different candidate compounds, each cell sample containing a predefined number of identical cells under conditions wherein said contacting is effected with a predetermined concentration of each different candidate compound to be tested.

75. A method of modulating MAT II β subunit biological activity in a vertebrate subject, the method comprising administering to the vertebrate subject an MAT II β subunit activity-modulating amount of a composition, whereby MAT II β subunit within the vertebrate subject is contacted by the composition; and modulating MAT II β subunit biological activity through the contacting of the MAT II β subunit with the composition.

76. The method of claim 75, wherein the composition comprises a monoclonal antibody which preferentially binds MAT II β subunit.

77. The method of claim 76, wherein the MAT II β subunit biological activity-modulating amount of the monoclonal antibody ranges from about 0.1
5 to about 300 milligrams per kilogram body weight of the vertebrate subject.

78. The method of claim 77, wherein the MAT II β subunit biological activity-modulating amount of the monoclonal antibody ranges from about 0.2 to about 200 milligrams per kilogram body weight of the vertebrate subject.

79. The method of claim 78, wherein the MAT II β subunit biological
10 activity-modulating amount of the monoclonal antibody ranges from about 0.5 to about 20 milligrams per kilogram body weight of the vertebrate subject.

80. The method of claim 76, wherein the antibody is humanized.

81. The method of claim 75, wherein the administering is selected for
15 the group consisting of intravenous administration, intrasynovial administration, transdermal administration, intramuscular administration, subcutaneous administration and oral administration.

82. The method of claim 75, wherein the vertebrate subject is a mammal.

83. The method of claim 82, wherein the mammal is a human.

20 84. A method of treating modulate MAT II β subunit biological activity in a vertebrate subject, the method comprising the step of administering to the vertebrate subject an effective amount of a substance capable of modulating expression of a MAT II β subunit-encoding nucleic acid molecule in the

vertebrate to thereby modulate MAT II β subunit biological activity in the vertebrate subject.

5 85. The method of claim 84, wherein the substance that modulates expression of the MAT II β subunit-encoding nucleic acid molecule comprises an antisense oligonucleotide.

10 86. The method of claim 84, wherein the substance that modulates expression of the MAT II β subunit-encoding nucleic acid molecule comprises a ligand for a modulatable transcriptional regulatory sequence of a MAT II β subunit-encoding nucleic acid molecule or for a promoter of the MAT II β subunit-encoding nucleic acid molecule.

 87. The method of claim 84, wherein the administering is selected for the group consisting of intravenous administration, intrasynovial administration, transdermal administration, intramuscular administration, subcutaneous administration and oral administration.

15 89. The method of claim 84, wherein the vertebrate subject is a mammal.

 90. The method of claim 88, wherein the mammal is a human.

20 91. A pharmaceutical composition comprising a therapeutically effective amount of a MAT II β subunit biological activity modulator and a pharmaceutically acceptable diluent or vehicle.

 92. The pharmaceutical composition of claim 89, wherein the MAT II β subunit biological activity-modulator is selected from the group consisting of a purified antibody which preferentially binds MAT II β subunit, or a fragment or derivative thereof, and a polypeptide, or a fragment or derivative thereof.

93. The pharmaceutical composition of claim 92, wherein the purified antibody is a monoclonal antibody, or fragment or derivative thereof.

94. The pharmaceutical composition of claim 93, wherein the monoclonal antibody is humanized.

5 95. A pharmaceutical composition comprising a therapeutically effective amount of a MAT II β subunit polypeptide, or a fragment or derivative thereof, and a pharmaceutically acceptable diluent or vehicle.